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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/586,026	07/13/2006	**Wenping Wu**	10515.204-US	7916

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EXAMINER	
SAIDHA, TEKCHAND	
ART UNIT	**PAPER NUMBER**
1652	
MAIL DATE	**DELIVERY MODE**
10/02/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/586,026	WU ET AL.	
	Examiner	Art Unit	
	Tekchand Saidha	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *9/5/2008 (telephone election)*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26-45* is/are pending in the application.

4a) Of the above claim(s) *34-45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/13/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claim amendment filed August 18, 2008 is acknowledged.

The numbering of claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

Misnumbered claims 37-43 been renumbered 39-45.

2. As per new numbering claims 26-45 are present.

3. Restriction is required under 35 U.S.C. 121 and 372, before a detailed first office action on the merits.

4. This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

5. In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 26-33, drawn to a fungal polypeptide of SEQ ID NO: 2 having lysozyme activity and a non-recombinant method of making the polypeptide recombinantly.

Group II, claim(s) 34-45, drawn to nucleic acid encoding the polypeptide of Group I.

6. The inventions listed as Groups I-II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical feature for the following reasons: The technical feature linking Groups I-II appears to be that they all relate to a lysozyme of SEQ ID NO: 1 or a fragment thereof, with no limitation to the size of the fragment. According to the international preliminary examination report [IPER] clams 1, 7-12 lack novelty as being anticipated by Felch et al. [JBC 250(10): 3713-3720, 197, (1975), cited in PTO-1449] and this is applicable to the amended claim 26 which recites such a fragment.

Therefore, Groups I-II share no special technical feature as defined by PCT Rule 13.2, as it does not define a contribution over the prior art.

Further, the DNA encoding the lysozyme of Group II and lysozyme of Group II are chemically and biologically distinct molecules. The enzyme and DNA have fundamentally different molecular structure, each with its own set of functionality. Enzyme, for example is biologically active, whereas DNA encoding the enzyme, is not. Additionally, the DNA constitutes the genetic material and is composed of the genes, and has other functions besides encoding the enzyme. Since the lysozyme and the DNA are biologically and chemically distinct, the manner of using the DNA may not necessarily involve the enzyme.

7. During a telephone conversation with Kristine McNamara on 9/5/2008 a provisional election was made with traverse to prosecute the invention of Group I, claim 26-33. Affirmation of this election must be made by applicant in replying to this Office action.

8. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

9. **Claims withdrawn** :

Claims 34-45 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

10. ***Priority***

Acknowledgment is made of applicants' claim for priority based on an application filed in Denmark on 2/25/2004.

Applicant's claim for domestic priority under 35 U.S.C. 119(e), filed 3/4/2004, is acknowledged.

11. ***Specification***

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

12. Claim 32 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 31. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

It appears to be a inadvertent error. Cancellation of one of the claims is suggested to overcome this objection.

13. ***Claim Rejections - 35 USC § 112*** (first paragraph)

Written Description

Claims 26-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants are directed toward the USPTO Written Description Training Materials made available to the public on 04/11/2008 for information regarding examination of patent claims for compliance with the written description requirement of 35 U.S.C. 112, first paragraph.

According to MPEP 2163, to satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. See, e.g., *Moba, B.V. v.Diamond Automation, Inc.*, 325 F.3d 1306, 1319, 66 USPQ2d 1429, 1438 (Fed.Cir. 2003); *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d at 1563, 19 USPQ2d at 1116.

The specification discloses the reduction to practice of one species within the claimed genus; specifically, the protein having the amino acid sequence of SEQ ID NO: 2. There are no drawings or structural formulas disclosed of any other protein having

the lysozyme activity. There is no teaching in the specification regarding the 5%-20% structure can be varied while retaining the ability of the protein to have lysozyme activity. Further, there is no art recognized correlation between any structure (other than SEQ ID NO: 2) and the lysozyme activity. Consequently there is no information about which amino acids can vary from SEQ ID NO: 2 in the claimed genus and still retain the catalytic activity.

Although the disclosure of SEQ ID NO: 2 combined with the knowledge would put one in possession of proteins that are at least 80-95% identical to SEQ ID NO: 2, the level of skill and knowledge in the art is such that one of ordinary skill would not be able to identify without further testing which of those proteins having at least 80-95% identity to SEQ ID NO: 2 (if any), and have lysozyme activity. Based on the lack of knowledge and predictability in the art, those of ordinary skill in the art would not conclude that Applicant was in possession of the claimed genus of proteins based on the disclosure of the single species of SEQ ID NO: 2.

MPEP § 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. In this case, the specification fails to disclose additional proteins having lysozyme activity, encompassed by the claims. As such the disclosure of the above mentioned *protein of SEQ ID NO: 2* is insufficient to be representative of the attributes and features common to all the members of each claimed genus. Thus, one skilled in the art cannot visualize or recognize the identity of the members of each claimed genus. In view of the above considerations, one of skill in the art would not recognize that applicants were in possession of the invention recited in claims 26-29.

14. ***Enablement Rejection***

Claims 26-29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polypeptide sequence of SEQ ID NO: 2, or a sequence which is 99% identical to the sequence of SEQ ID NO: 2 or a method of non-recombinant production of sequence of SEQ ID NO: 2, does not reasonably provide

enablement for any polypeptide having 80-95% identity to SEQ ID NO: 2 and having lysozyme activity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The scope of the claims does not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polypeptides broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide [SEQ ID NO: 1] and encoded amino acid sequence of SEQ ID NO: 2.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications of protein of SEQ ID NO: 2 by 5-20%, because the specification does **not** establish: (A) regions of the protein structure which may be modified without effecting lysozyme activity; (B) the general tolerance of the lysozyme to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any lysozyme residues with an expectation of obtaining the desired enzymatic or biological function capable of catalyzing a defined chemical reaction using known

substrates; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus there is high unpredictability associated with respect to modification(s) of the sequence of SEQ ID NO: 1 or 2 unless guidance is provided in establishing (A) – (D) as discussed above.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of exact nature of the encoding DNA (or polynucleotide) encoding a specific protein having lysozyme activity of known substrate specificity having the desired enzymatic characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

15. ***Deposit Requirement***

Claims 26-33 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that the [plasmid/microorganism/vector] is required to practice the claimed invention. As such the [plasmid/microorganism/vector] must be readily available or obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public. If it is not so obtainable or available, the requirements of 35 U.S.C. 112, first paragraph, may be satisfied by a deposit of the [plasmid/microorganism/vector]. The specification lacks complete deposit information for the deposit of [plasmid/microorganism/vector]. If a deposit was made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicants, or a statement by an attorney of record over his or her signature and registration number, stating that the instant invention will be irrevocably and without restriction released to the public upon

the issuance of a patent, would satisfy the deposit requirement made herein. If a deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809 and MPEP 2402-2411.05, Applicant may provide assurance of compliance by affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number showing that (a) during pendency of the application, access to the invention will be afforded to the Commissioner upon request, (b) all restrictions upon availability to the public will be irrevocable removed upon granting of the patent, (c) the deposit will be maintained in a public depository for a period of 30 years, or 5 years after the last request or for the enforceable life of the patent, whichever is longer, (d) a test of the viability of the biological material at the time of deposit (see 37 CFR 1.807) and (e) the deposit will be replaced if it should ever become inviable.

In the instant case the strain DSM16084 contains nucleotides 84-782 of SEQ ID NO: 1 [claim 26(b)], for which the deposit criteria set forth in 37 CFR 1.801-1.809 is not satisfied. Claims 27-33 are included in the rejection for failing to correct the defect present in the base claim.

Claims 26-33 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

16. **35 U.S.C. § 101**

35 U.S.C. § 101 reads as follows:

"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

Claims 26-33 are rejected under 35 U.S.C. § 101 because the claimed invention is directed toward non-statutory subject matter.

In the absence of the hand of man, naturally occurring proteins and/or nucleic acids are considered non-statutory subject matter. *Diamond v. Chakrabarty*, 206 USPQ 193 (1980). This rejection may be overcome by amending the claim 26 to recite wording such as "An isolated fungal polypeptide".

Claims 27-33 are included in the rejection for failing to correct the defect present in the base claim.

17. ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 26 is rejected under 35 U.S.C. 102(b) as being anticipated by Felch et al. [JBC 250(10): 3713-3720, 197, (1975), cited in **PTO-1449**] and this is applicable to the amended claim 26 which recites such a fragment. Felch et al. teach a lysozyme (Accession Number. A00876) having several fragments of varying lengths that match different portions fragments of SEQ ID NO: 2, and therefore anticipates claim 26 which recites fragment of any size. Further, various fragments used in sequencing are disclosed in Table 1.

```
lysozyme (EC 3.2.1.17) - fungus (Chalara sp.)
N;Alternate names: lysozyme Ch; N,O-diacetylmuramidase
C;Species: Chalara sp.
C;Date: 24-Apr-1984 #sequence_revision 24-Apr-1984 #text_change 09-Jul-2004
C;Accession: A00876
R;Felch, J.W.; Inagami, T.; Hash, J.H.
J. Biol. Chem. 250, 3713-3720, 1975
A;Title: The N,O-diacetylmuramidase of Chalaropsis species. V. The complete amino acid sequence.
A;Reference number: A92178; MUID:75151523; PMID:1168638
A;Accession: A00876
A;Molecule type: protein
A;Residues: 1-211
A;Cross-references: UNIPROT:P00721; UNIPARC:UPI000012EA38
A;Note: this is the final paper in a series
R;Fouche, P.B.; Hash, J.H.
J. Biol. Chem. 253, 6787-6793, 1978
A;Title: The N,O-diacetylmuramidase of Chalaropsis species. Identification of aspartyl and glutamyl residues in the
active site.
A;Reference number: A92236; MUID:79005662; PMID:567645
A;Contents: annotation; active site
C;Comment: This extracellular enzyme has both lysozyme (acetylmuramidase) and diacetylmuramidase activities.
C;Function:
A;Description: catalyzes hydrolysis of the beta-1,4-glycosidic bond between N-acetylmuramic acid and N-
acetylglucosamine in peptidoglycan and other complex polysaccharides
C;Superfamily: Chalara lysozyme; Chalara lysozyme homology
C;Keywords: extracellular protein; glycosidase; hydrolase
F;6-170/Domain: Chalara lysozyme homology
F;6,33/Active site: Asp, Glu #status experimental
F;108-147/Disulfide bonds: #status experimental

  Query Match            52.2%;  Score 654;  DB 1;  Length 211;
  Best Local Similarity  56.9%;  Pred. No. 2.4e-43;
  Matches  119;  Conservative   33;  Mismatches   53;  Indels    4;  Gaps    2;

Qy         29 KGIDVSAYQPNINWSTVKANGISFAYIKATEGTTYTNPDFSSQYTGATNAG---LIRGGY 85
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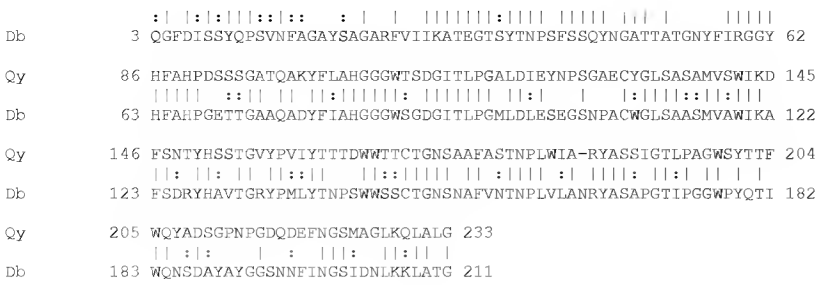

18. No claim is allowed.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tekchand Saidha whose telephone number is (571) 272 0940. The examiner can normally be reached between 8.30 am - 5.00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nashaat Nashed can be reached on (571) 272 0934. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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